REMARKS

Claims 1 and 13 were previously pending in this application; new claims 14-18 have been added. Support for new claims 14-18 can be found in the specification, for example, at page 55, lines 9-23. The specification has been amended at the request of the Examiner to remove hyperlinks and browser executable code. No new matter enters by way of these amendments.

Applicants note that the Examiner has withdrawn the finality of the office action.[1] Applicants also note that Applicants' amendment and request for reconsideration in Paper #26, filed on January 16, 2003, has been entered and Applicants' appeal brief has been acknowledged.

I. Specification

The specification has been objected to because it allegedly contains an embedded hyperlink and/or other form of browser executable code. According to M.P.E.P. §608.01, embedded hyperlinks and browser executable code are not permitted. The specification has been amended to remove the phrase "http://." No new matter has been added by this amendment. Applicants request that the objection to the specification be withdrawn.

II. Claim Rejections – 35 U.S.C. § 101

Claims 1 and 13 have been rejected under 35 U.S.C. § 101 as allegedly lacking patentable utility due to not being supported by a specific, substantial, and credible utility, or, in the alternative, a well-established utility. Office Action page 3. Applicants respectfully disagree.

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1 Applicants presume that the Examiner means that the finality of the Final Office Action mailed August 27, 2002, has been withdrawn, rather than the finality of the application.

The Examiner contends that "[t]he claims would reasonably be interpreted to mean either (1) that SEQ ID NO: 1 encodes the entire enzyme of maize methionine adenosyltranferase or (2) that its entirety encodes a fragment of the enzyme, i.e. every part of SEQ ID NO: 1 encodes a portion of the enzyme, or (3) that it contained a nucleotide sequence that encodes a fragment of the enzyme." Office Action page 3. The Examiner further contends that "[a] search of SEQ ID NO: 1 suggests that SEQ ID NO: 1 is a hybrid sequence containing elements from a 'cDNA encoding corn protein phosphatase 2A regulatory subunit A' and a 'cDNA homologous to methionine adenosyltransferase.' " Office Action page 3.

While the Examiner proceeds to analyze SEQ ID NO: 1 by comparing it to the results of various art searches, the Examiner has failed to show that SEQ ID NO: 1 does not function as described by the specification. The Examiner provides only a bare allegation that SEQ ID NO: 1 will function in the same way that various similar nucleic acid sequences in the art function. However, the Examiner has failed to provide evidence that SEQ ID NO: 1 does not function in the manner described by the specification.

The specification provides extensive evidence based on sequence identity (Table A) that the claimed nucleic acid molecules encode a polypeptide having 92% identity to a known methionine adenosyltransferase. *See, e.g.*, Table A, at page 226, line corresponding to SEQ ID NO: 1. The specification also indicates by way of EC Classification designation that the specified enzyme is of an enzymatic classification well-known in the art. Further, a detailed description of the characterization of the specified enzyme, as well as the identification of such enzyme from other plant sources is provided in the specification. *See, e.g.*, specification at page 10-11. As such, it is submitted that the functionality of the claimed nucleic acid molecules is

disclosed. Further, based on the background provided regarding the functionality and structural characteristics of the claimed enzyme, it is submitted that sequence homology is indeed an adequate and predictable indicator of such functionality. Thus, based on such teachings, one of ordinary skill in the art would immediately appreciate the usefulness of the claimed nucleic acid molecules.

An examiner must accept a utility asserted by an applicant unless the Office has evidence or sound scientific reasoning to rebut the assertion. *See In re Oetiker*, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992). "More specifically, when a patent application claiming a nucleic acid asserts a specific, substantial, and credible utility, and bases the assertion upon homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted by the examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such an assertion." Federal Register 66(4):1096, Utility Guidelines (2001). "[A] 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' is sufficient." *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1565, 39 U.S.P.Q.2d 1895, 1900 (Fed. Cir. 1996).

As such, an examiner "must do more than question operability – [the examiner] must set forth factual reasons which would lead one skilled in the art to question the objective truth of the statement of operability." *In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975); *see In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995); M.P.E.P. § 706.03(a)(1). No such factual reasons have been provided. The utilities disclosed by Applicants must be accepted as factually sound unless and until the Patent Office

provides factual reasons that undermine the credibility of the assertion. Therefore, the Office has not met the requisite burden to impose a 35 U.S.C. § 101 rejection.

Based on his search of the prior art, the Examiner further contends that "a prima facie case exists that SEQ ID NO: 1 is neither the complete sequence of methionine adenosyltransferase or a fragment thereof...[and]...the assertion that SEQ ID NO: 1 encodes the entire maize methionine adenosyltransferase or the entirety encodes a fragment of the enzyme lacks factual basis." Office Action page 4. Again, the Examiner fails to provide conclusive proof to support his allegation. Rather, the Examiner appears to support his allegation for lack of utility by comparing fragments of SEQ ID NO: 1 to fragments of known nucleic acid sequences. First, Applicants respectfully point out that novelty *requires* that a claimed nucleic acid molecule *not appear* in the prior art in its entirety. Second, as previously stated, Table A on page 224 of the specification shows a 92% sequence identity between the translated product of SEQ ID NO: 1 and a known methionine adenosyltransferase. Thus, Applicants assert that the 92% homology to a known methionine adenosyltransferase is sufficient to show the functionality of the claimed nucleic acid molecules within the scope of the claimed invention.

Applicants have also previously asserted that the claimed nucleic acid molecules can be used, for example, to identify polymorphisms, as probes for other molecules, and as molecular markers. *See, e.g.*, Appeal Brief dated January 27, 2003, at pages 4-10, and specification, for example, at page 74, line 5 through page 75, line 15; page 76, line 20 through page 84, line 13; and page 84, line 14 through page 89, line 17.

The Examiner argues that these uses are not specific and substantial. Office Action page 5. Applicants respectfully disagree. The Examiner has provided no evidence, or even a reason to

suggest that the claimed nucleic acid molecules could not be used for these or other disclosed utilities.

Because the disclosed utilities are not incredible and are based on sound scientific reasoning, the Examiner has not met the burden to impose a utility rejection. Thus, reconsideration and withdrawal of the rejection under 35 U.S.C. § 101 is respectfully requested.

III. Claim Rejections – 35 U.S.C. § 112, first paragraph, enablement

Claims 1 and 13 have been rejected under 35 U.S.C. 112, first paragraph, as allegedly lacking patentable utility due to allegedly not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility. Office Action page 5. Applicants respectfully disagree, and note that this rejection has been overcome by the foregoing arguments regarding utility. Thus, the enablement rejection under 35 U.S.C. § 112, first paragraph, is improper. Reconsideration and withdrawal are respectfully requested.

IV. Claim Rejections – 35 U.S.C. § 112, first paragraph, enablement

Claims 1 and 13 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner cites *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1998) and the eight factors to be considered in a determination of "undue experimentation."

A reasonable analysis of the *In re Wands* criteria also supports Applicants' position that no undue experimentation would be required to make and use the claimed invention. *See In re*

Wands, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1998). The first *Wands* criterion is the quantity of experimentation necessary. The "make-and-test" quantum of experimentation is reduced by the extensive knowledge, *e.g.*, of conservative nucleotide substitutions, identification of an active site, and radiometric synthase assay conditions, to which a person of ordinary skill in the art has access. Performing routine and well-known steps, such as sequence alignment protocols, molecular weight determination, and antibody hybridization assays, cannot create undue experimentation even if it is laborious. *See In re Angstadt*, 537 F.2d 498, 504, 190 U.S.P.Q. 214, 218-219 (C.C.P.A. 1976).

Moreover, as discussed *supra*, the specification provides evidence based on sequence identity (Table A) that the disclosed genes encode polypeptides, or fragments thereof, having methionine adenosyltransferase activity. Additionally, the specification teaches that the methionine adenosyltransferase enzyme has been characterized from several plant sources, and that nucleic acid molecules have been obtained from a variety of sources. *See, e.g.,* specification at pages 10-11. Further, the specification discloses that the regulation of methionine adenosyltransferase activity has been observed for an enzyme from soybean, and that the functionality of methionine adenosyltransferase has been experimentally characterized. *See, e.g., Id.* at page 11. As such, it is submitted that sequence homology is indeed an adequate and predictable indicator of methionine adenosyltransferase functionality, and that one of ordinary skill in the art would clearly understand from the teachings of the specification that the claimed nucleic acid sequences have methionine adenosyltransferase activity without the need for undue experimentation.

The second and third *Wands* criteria relate to the amount of direction or guidance given, and the presence or absence of working examples. Again, the specification provides evidence of sequence identity and discloses general characterizations of methionine adenosyltransferase. The Examiner alleges that "the entire sequence of SEQ ID NO: 1 appears to be a hybrid of phosphatase 2A regulatory subunit A and methionine adenosyltransferase." Office Action page 6. However, the Examiner ignores Applicants' disclosure that SEQ ID NO: 1 encodes a polypeptide having 92% identity to a known methionine adenosyltransferase or fragment thereof. *See* Table A. Based on such disclosure, one of ordinary skill in the art would be enabled to make and use the invention commensurate in scope with the claims.

The fourth, fifth, and sixth *Wands* criteria focus on the nature of the invention, the state of the art, and the relative skill in the art. The present invention relates to nucleic acid and amino acid sequences, and constructs and methods related thereto. Applicants thank the Examiner for acknowledging that SEQ ID NO: 1 is not known in the prior art. Office Action page 7. However, this fact does not support an allegation that a nucleic acid molecule comprising SEQ ID NO: 1 would require undue experimentation for the disclosed utilities. Practitioners in this art are guided by considerable knowledge and resources on the conditions and approaches that can be utilized to identify, confirm, and introduce into other hosts, nucleic acid and amino acid sequences. *See*, for example, specification at page 119, line 19 through page 120, line 10 (citing references for the development of assays to detect gene expression for the claimed nucleic acid molecules).

The seventh criterion considers the predictability of the art. The Examiner alleges a level of uncertainty involving a functional assignment of metabolic genes based on homology between

known and unknown genes. Office Action page 7. Applicants respectfully disagree and assert, as discussed *supra*, that the specification discloses sufficient guidance to render the results predictable.

The eighth criterion focuses on the breadth of the claims. Enablement is satisfied when the disclosure "adequately guide[s] the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility." *See In re Vaeck,* 947 F.2d 488, 496, 20 U.S.P.Q.2d 1438, 1445 (Fed. Cir. 1991). In the present case, one of skill in the art is specifically guided by the disclosure to look to, *e.g.*, sequence identity data, functional assay, and EC classification, in making that determination. Furthermore, the Examiner alleges that the "practitioner would turn to trial and error experimentation for using the claimed polynucleotides..." However, performing routine and well-known steps, such as those discussed above and disclosed throughout the present specification, cannot create undue experimentation, even if it is laborious. *See In re Angstadt*, 537 F.2d. at 504.

Accordingly, for at least these reasons, Applicants disagree with the enablement rejection under 35 U.S.C. § 112, first paragraph, and respectfully request withdrawal of this rejection.

V. Claim Rejections – 35 U.S.C. § 112, first paragraph, written description

Claim 1 has been rejected under 35 U.S.C. §112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Initially, the purpose of the written description requirement is simply to ensure that the inventors had possession of the claimed subject matter, *i.e.*, to ensure that the inventors actually invented what is claimed. *See Gentry Gallery Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *Lockwood v. American Airlines*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997); *In re Alton*, 76 F.3d 1168, 1172, 37 U.S.P.Q.2d 1578, 1581 (Fed. Cir. 1996). In accordance with this purpose, Applicants need not "describe," in the sense of Section 112, all things that are encompassed by the claims. To contend otherwise would contradict established jurisprudence, which teaches that a patent may be infringed by technology developed after a patent issues. *United States Steel Corp. v. Phillips Petroleum Co.*, v865 F.2d 1247, 1251, 9 U.S.P.Q.2d 1461, 1464 (Fed. Cir. 1989).

A related and equally well-established principle of patent law is that claims "may be broader than the specific embodiment disclosed in a specification." *Ralston Purina Co. v. Far-mor-Co*, 772 F.2d 1570, 1575, 227 U.S.P.Q. 177, 179 (Fed. Cir. 1985) (*quoting In re Rasmussen*, 650 F.2d 1212, 1215, 211 U.S.P.Q. 323, 326 (C.C.P.A. 1981)). Thus, simply because the claimed nucleic acid sequences may also include sequences from other species does not require that Applicants describe each and every one of these molecules. Further, "a description as filed is presumed to be adequate, unless and until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption." *Federal Register* 66(4):1107, Written Description Guidelines (2001). In this regard, the Examiner is required to disclose "express findings of fact which support the lack of written description conclusion." *Id.*

The present claims are directed to, for example, a substantially purified nucleic acid molecule that encodes a maize enzyme or fragment of said maize enzyme, wherein said maize

enzyme is Methionine Adenosyltransferase and wherein said nucleic acid molecule comprises the nucleic acid sequence of SEQ ID NO: 1. Applicants have provided detailed chemical structures of the claimed nucleic acid sequence, as well as additional information about the encoded enzyme. This sequence provides "structural feature[s] possessed by members of the [claimed] genus that distinguish them from others." *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997). In contrast to the mere name "cDNA" provided in *Eli Lilly*, Applicants have provided detailed chemical structures. For at least this reason, it is respectfully submitted that the present claims meet the written description provision under 35 U.S.C. § 112, first paragraph.

The use of open claiming language (comprising) or semi-open claiming (consisting essentially of) does not alter the fact that a skilled artisan would readily envision adequate written description support. Contrary to the allegations raised in the Office Action regarding the "substantial variability" among the claimed species, it is submitted that the claimed species are adequately defined by the recitation of the specific sequence of SEQ ID NO: 1. As such, the claims do not encompass "any full-length gene or cDNA species, or any vector," rather the claims encompass only those molecules which include the structural sequence of SEQ ID NO: 1. The fact that nucleic acid sequences may be added to either end of the recited sequence is beside the point. Applicants have therefore reasonably conveyed to one skilled in the art possession of the claimed invention, even when additional sequences are added to either end. For example, as disclosed in the specification on page 53, the addition of, *e.g.*, detectable labels or extra nucleotides is readily envisioned by those of ordinary skill upon reading the present specification.

Additionally, "it may not be necessary to enumerate a plurality of species if a genus is sufficiently identified in an application by 'other appropriate language.' " *Eli Lilly*, 119 F.3d at 1569. In the present case, although Applicants were restricted to examination of SEQ ID NO: 1, it is submitted that the disclosure of an extensive number of nucleic acid sequences encoding the specified enzyme or fragments thereof, *e.g.,* SEQ ID NOS: 1-429 and 1635-2479, in combination with "other appropriate language" in fact does provide sufficient written description for claims within the genus. Such "other appropriate language" is found, *e.g.*, in the form of sequence identity and numerous methodologies to obtain additional sequences. Therefore, it is clear that one of ordinary skill in the art would recognize that Applicants were in possession of the claimed invention.

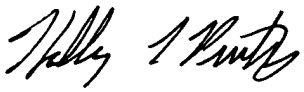
Accordingly, for at least the foregoing reasons, the rejection under 35 U.S.C.. §112, first paragraph, written description, is traversed, and withdrawal of this rejection is respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is now in condition for allowance, and notice of such is respectfully requested.

The Examiner is encouraged to contact the undersigned should any additional information be necessary for allowance.

Respectfully submitted,



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